

### **REMARKS**

Applicants respectfully request reconsideration and withdrawal of the outstanding objections and rejections, in light of the foregoing amendments and following remarks.

#### **Status of Claims**

Claims 33-36, 38-41 and 47-50 are allowed.

Claims 1, 7, 14, 19-23, 37 and 46 have been amended.

Claims 42-45 and 54 have been canceled without prejudice.

Claims 1-41 and 46-53 are now pending for the Examiner's consideration.

For the reasons that follow, Applicants believe all Claims are now in condition for allowance.

#### **Allowable Subject Matter**

Applicants acknowledge with appreciation that Claims 33-36, 38-41 and 47-50 are allowed.

The Examiner also indicates that Claims 2-6, 8-13, 15-18, 24-32 and 51-53 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. However, Applicants have amended the base Claims 1, 7, 14, 19-23, 37 and 46 upon which Claims 2-6, 8-13, 15-18, 24-32 and 51-53 are dependent to overcome the sole 35 U.S.C. § 112, the first paragraph rejection, as shown below. Accordingly, Applicants believe that there is no need to rewrite Claims 2-6, 8-13, 15-18, 24-32 and 51-53, which are now in condition for allowance.

#### **Title**

The Office alleges that the title of the invention is not descriptive. Applicants contend that the title of the invention is clearly indicative of the invention to which the claims are directed. However, in order to expedite prosecution of the present application, Applicants have amended the title as suggested by the Examiner to add the word "Fused" to the beginning of the present title. No new matter is added by the way of this amendment.

#### **Specification**

The Office alleges that "[t]he attempt to incorporate subject matter into this application by reference to Brinstock et al., *Methods Enzymol.*, 71, 403-411, 1981 on page 100 is improper because this is essential material for anyone trying to practice Applicants invention." Applicants respectfully disagree with this allegation for the following reasons.

First, Applicants cite the Brinstock et al. reference in the "BIOLOGICAL TESTING: ERAB ENZYME ASSAY" section on page 100, lines 3-5 in order to indicate that:

"The activity of ERAB (L-3-hydroxyacyl-CoA dehydrogenase) in the reverse direction was determined by a ***modified version*** of a method previously described (Binstock et al., *Methods Enzymol.*, 71, 403-411 (1981))." (emphasis added).

Second, Applicants give a detailed description of their method and assay conditions for determining the IC<sub>50</sub> value for compounds of the Formula I at page 100, lines 5 through 24 of the

originally-filed application, thus providing the essential material for anyone trying to practice Applicants' invention. Accordingly, there is no improper incorporation of essential material in the specification by reference to a publication. Applicants respectfully request that a requirement to amend the disclosure to include the material incorporated by reference be withdrawn.

**Rejection under 35 U.S.C. § 112, the second paragraph**

Claim 42 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because it is allegedly unclear what diseases and treatments applicant is intending to encompass.

Applicants believe that the originally-filed application provides the sufficient disclosure in identifying a disease or condition mediated by ERAB, HADH2, or amyloid- $\beta$ , for example, at page 2, lines 14-21; at page 3, line 22 through page 6, line 7. However, in order to expedite prosecution of the present application Applicants have canceled Claim 42 without prejudice. Cancellation of Claim 42 does not constitute any admission regarding the subject matter of Claim 42. Applicants reserve a right to pursue the subject matter of Claim 42 in this or other application(s).

In view of cancellation of claim 42, Applicants respectfully request that the rejection be withdrawn.

**Rejection under 35 U.S.C. § 112, the first paragraph**

Claims 1, 7, 14, 19-23, 37, 42-46, and 54 were rejected under 35 U.S.C. § 112, the first paragraph, as being allegedly not enabling for making prodrugs or metabolites of the claimed compounds. This rejection is moot in regard to Claims 42-45 and 54 because of their cancellation.

As to Claims 1, 7, 14, 19-23, 37, and 46, Applicants note that the direction concerning the prodrugs and metabolites, in addition to page 22, lines 24-27 cited by the Office, can be found also, for example, at page 38, lines 11-24. Thus, the specification provides enablement for making prodrugs or metabolites of the claimed compounds by teaching, *inter alia*, that:

"Prodrugs and active metabolites of a compound may be identified using routine techniques known in the art. See, e.g., Bertolini et al., *J. Med. Chem.*, 40, 2011-2016 (1997); Shan et al., *J. Pharm. Sci.*, 86 (7), 765-767; Bagshawe, *Drug Dev. Res.*, 34, 220-230 (1995); Bodor, *Advances in Drug Res.*, 13, 224-331 (1984); Bundgaard, *Design of Prodrugs* (Elsevier Press 1985); Larsen, *Design and Application of Prodrugs, Drug Design and Development* (Krogsgaard-Larsen et al., eds., Harwood Academic Publishers, 1991); Dear et al., *J. Chromatogr. B*, 748, 281-293 (2000); Spraul et al., *J. Pharmaceutical & Biomedical Analysis*, Vol. 10, No. 8, 601-605 (1992); and Prox et al., *Xenobiol.*, Vol. 3, No. 2, 103-112 (1973)." Page 38, lines 15-24.

However, in order to expedite prosecution of the present application Applicants have amended Claims 1, 7, 14, 19-23, 37 and 46 by deleting "a pharmaceutically acceptable prodrug, or a pharmaceutically active metabolite of said compound, or a pharmaceutically acceptable salt of said metabolite" from the language of the claims. This amendment of Claims 1, 7, 14, 19-23, 37 and 46, does not constitute any admission regarding prodrugs or metabolites of the claimed

compounds. Applicants reserve a right to pursue this subject matter in this or other application(s).

By the present amendments, Applicants believe the rejection has been overcome, and respectfully request that the rejection be withdrawn.

**Rejection under 35 U.S.C. § 112, the first paragraph**

Claims 42-45 and 54 were rejected under 35 U.S.C. § 112, the first paragraph, as being allegedly not enabling for treating any human disease.

Applicants note that the direction concerning methods of treating diseases mediated by ERAB can be found, for example, at page 2, lines 14-21 and page 3, line 22 through page 6, line 7 of the originally-filed application.

However, in order to expedite prosecution of the present application Applicants have canceled Claims 42-45 and 54. Cancellation of Claims 42-45 and 54 does not constitute any admission regarding the subject matter of Claims 42-45 and 54. Applicants reserve a right to pursue the subject matter of Claims 42-45 and 54 in this or other application(s).

In view of cancellation of claim 42, Applicants respectfully request that the rejection be withdrawn.

**Conclusion**

Applicants believe all claims are now in condition for allowance. Should there be any issues that have not been addressed to the Examiners satisfaction, Applicants invite the Examiner to contact the undersigned attorney.

If any fees other than those submitted herewith are due in connection with this response, please charge such fees to Deposit Account No. 500329.

Respectfully submitted,

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